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LETTER TO THE EDITOR

We are pleased to receive Letters to the Editor on appropriate subjects. These letters should be submitted in typewritten form, double-spaced, and are not to exceed 2½ pages. When appropriate, we will solicit comments from the original authors. All Letters to the Editor are subject to editing and possible abridgment.

PUVA-INDUCED UVB-TUMOR SUSCEPTIBILITY

To the Editor:

We were extremely interested in the recent report by Kripke, Morison, and Parrish [1] concerning short wave ultraviolet light (UVB) induced tumor susceptibility in mice treated with either UVB or 8-methoxypsoralen plus UVA (PUVA). Since their results diametrically oppose our earlier findings [2], we felt compelled to clarify the major difference between the two methodologies employed.

Previous reports from both laboratories [3, 4] have established that UVB-regressor (UVB^r) tumors, while rejected by normal syngeneic mice, are capable of progressive growth in UVB-treated hosts. This UV-induced tumor-susceptible state is known to be mediated by antigen specific (Roberts et al, manuscript in preparation [5], radiosensitive, Ia^+, suppressor T-lymphocytes [6]. In both studies [1, 2], experiments were designed to determine if PUVA treatments would mimic the effects of UVB by rendering mice susceptible to UVB^r-tumor growth. We reported [2] that PUVA-treated mice supported UVB^r-tumor growth and presented evidence suggesting Ia^+, suppressor-cell involvement. In contrast, Kripke, Morison and Parrish [1] found that PUVA treated mice behaved like normal animals and rejected UVB^r tumors. Although Kripke, Morison and Parrish attempted to approximate our experimental protocol [2], their UVA irradiations were made with mylar filtered light rather than with UVA bulbs emitting their entire photospectrum. It is this difference between our two methodologies that accounts for the discrepancies in our results.

In their discussion, Kripke, Morison and Parish suggest two possible explanations for the discrepancy between their findings and ours. First, the authors suggest that immunologic debilitation due to infectious disease, secondary to the PUVA treatments, may have been of sufficient magnitude to permit tumor growth in our PUVA-treated mice. Although we have never published the microbial or viral status of our animals and tumors, both have been screened (for many of the same, and some additional, pathogens listed by Kripke, Morison, and Parrish) and were found to be pathogen free. Thus, this contention proves invalid. The second possibility, which in our opinion is far more intriguing and received too little attention in their discussion, reiterates the major difference between our two protocols, i.e., the use of filtered versus unfiltered UVA. In comparing our data [2] with that of Kripke, Morison, and Parrish [1] it would appear that, at least for the induction of UVB^r-tumor susceptibility, the effects mediated by PUVA may result from a synergism between 8-methoxypsoralen and the small amounts of short wave UV emitted by UVA bulbs rather than a true potentiation of long wave UV light (wave lengths greater than 320 nm). This aspect of PUVA-treatment and its effect on UVB-tumor susceptibility certainly requires further investigation.

We believe that our protocol [2] is more clinically relevant than that employed by Kripke, Morison and Parrish [1]. To our knowledge it is the full emission spectrum of the UVA bulbs, rather than mylar filtered light, that is used when treating psoriasis and vitiligo patients with PUVA. In addition, we strongly believe that our interpretations of experimental results presented previously [2, 7], and the available human data [8], suggest a link between cancer risk and tumor specific suppression induced by UVB and possibly PUVA [9].

Lee K. Roberts
University of New Mexico School of Medicine
Raymond A. Daynes
University of Utah Medical Center

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REPLY

It is helpful to know that the animals used by Roberts, Schmitts, and Daynes were pathogen free and that the authors agree with one of our suggested explanations for the discrepancy between their findings and ours. It would be unwise to overstate the clinical relevance of either study, even though we agree the use of unfiltered bulbs is common in clinical situations. However, the stated intention of their study was to investigate the effect of methoxsalen and UVA (320–400 nm) radiation. It would appear that by adopting the approach of using unfiltered bulbs, they have inadvertently investigated the effects of UVB radiation and even possibly an interaction between methoxsalen and UVB radiation. Obviously, further studies are required to dissect out the various influences that they have studied.

M. L. Kripke
W. L. Morison
Frederick Cancer Research Center
J. A. Parrish
Massachusetts General Hospital

CIRCADIAN RHYTHMS IN MITOTIC INDEX IN NORMAL AND PSORIATIC EPIDERMIS

Gelfant et al [1] in their recent report state "there are no circadian diurnal variations in epidermal cell proliferation" in uninvolved psoriatic skin.

I believe this should be amended to state that in the 12 biopsies taken each time from the male psoriatic volunteers comprising their experimental material, they found no circadian diurnal variation in mitotic index in the epidermis. We, however, have reported a very definite diurnal variation in mitotic index of normal human epidermis, and uninvolved epidermis of psoriatics, as we reported previously [2]. Our difference may relate to sample size.

More than by chance, and with high statistical significance [3], mitotic figures in adult human epidermis are found clustered. This occurs at different sites within the same 6-mm biopsy, and from biopsy to biopsy taken at the same time from the buttock area of the same individual. To obtain a mitotic index that represents the individual in view of this clustering, requires extensive sampling.

Gelfant et al compared findings at 4 times during 24 hr. However, in contrast to our findings, their table 1 shows no significant difference in mitotic index from 9 AM to 3 PM either.

However, we counted mitoses on 99 biospies in 33 psoriatics for 20 cm length of epidermis (40 sections) each biopsy, at 9 AM and 99 more biopsies at 3 PM for uninolved skin of psoriatics. Gelfant's [1] sample size was 12 biopsies counted for 10 cm length each at 9 AM and again at 3 PM.